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EXAMINER
WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,080	MORIN, GREGG B.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2 (in part), 3-4, 5-7 (in part), 10-15 (in part), 16 -17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-2 (in part), 5-7 (in part),10-15 (in part), 8-9 and 18-20 .

The Response to Restriction Requirement filed on Feb. 20, 2004 is acknowledged. Claims 1-20 are pending. Invention of Group II, Claims 1 and 1, 2, 5, 6, 7, 10, 11, 12, 13-15 all in part related to polypeptides comprising at least 10 consecutive amino acids of polypeptide encoded in a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a sequence complementary or SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565 residues 930-934, or at least 10 consecutive amino acids from residues 323-450, 637-660, 748-766, 1055-1071, or 1084-1116 of SEQ ID NO:2, as well as claims 3, 4, 16 and 17 are the subject of this Office Action.

DETAILED ACTION

1. Election/Restriction

Claims 1-2 (in part), 5-7 (in part), 8-9, 10-15 (in part) and 18-20, are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant's election without traverse of invention of Group II is acknowledged. Claims 1, 2, 5, 6, 7, 10, 11, 12, and 13-15 all in part related to polypeptides which have a sequence comprising at least 10 consecutive amino acids of polypeptide encoded in a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a sequence complementary or SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565, residues 930-934, or at least 10 consecutive amino acids from residues 323-450, 637-660, 748-766, 1055-1071, or 1084-1116 of SEQ ID NO:2, as well as claims 3, 4, 16 and 17 are under examination. Claims 1, 2, 5, 6, 7, 10, 11, 12, 13-15 all in part related to polypeptides comprising at least 10 consecutive amino acids of SEQ ID NO: 2 or a sequence that consists

essentially of SEQ ID NO: 3, 4 and 5 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. Objections

2.1. Specification

The specification is objected to for defining the term "corresponds" by using indefinite phrase "substantially identical" (page 12, line 3).

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors in the specification of which Applicant may become aware.

3. Rejections

3.1. 35 USC, section 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is directed to:

"A protein, peptide, or mimetic that inhibits human telomerase, which either

a) has a sequence comprising at least 10 consecutive amino acids in SEQ ID NO: 2, or encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a sequence complementary to SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565, residues 930-934, or at least 10 consecutive amino acids from residues 323-450, 637-660, 748-766, 1055-1071, or 1084-1116 of SEQ ID NO: 2; or

b) has a sequence consisting essentially of FFYVTE (SEQ ID NO: 3); FYVT (SEQ ID NO: 5), or at least 10 consecutive amino acids from YGVLLKTHCPLRAA (SEQ ID NO: 4)."

In their response to the restriction requirement Applicant writes:

"The claims being examined in part will be considered with respect to polypeptide encoded in a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a sequence complementary to complementary [the repetition of the adjective complementary is absent from the claim] to sequence SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565, 930-934, or at least 10 consecutive amino acids from residues 323-450, 637-660, 748-766, 1055-1071, or 1084-1116 of SEQ ID NO:2, and methods of using such polypeptides for inhibiting telomerase catalytic activity.

Because of this election claim 1 may read:

A. A protein, peptide, or mimetic that inhibits human telomerase, which either comprises at least 10 consecutive amino acids of a sequence encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting

of a sequence complementary to SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565, residues 930-934, **or** [comprises] at least 10 consecutive amino acids from residues 323-450,637-660, 748-766, 1055-1071, or 1084-116 of SEQ ID NO: 2 or

B. A protein, peptide, or mimetic that inhibits human telomerase, which comprises at least 10 consecutive amino acids of a sequence encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a sequence complementary to SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565, residues 930-934, or a deletion of at least 10 consecutive amino acids from residues 323-450, 637-660, 748-766, 1055-1071, or 1084-1116 of SEQ ID NO:2.

It is assumed for examination purposes that the proper version of the claim is B.

Claim 1 and 16 are rejected because the claim recites the phrase "hybridizes under stringent conditions" which renders the claim indefinite. There are many sets of stringent conditions in the prior art that are used for selecting DNA molecules by hybridization. The result of the hybridization experiment would vary with the conditions used, especially because the claimed polypeptide is encoded by a sequence that comprises several deletions in comparison with the sequence to which it hybridizes. The specification is silent about any hybridization conditions the Applicants intend to use.

Claim 5-7, 13-17 are rejected, because the claims are directed to a dominant negative mutant of human telomerase that inhibits telomerase activity. The meaning of the term "dominant negative mutant" comprises limitation "inhibits telomerase activity". In addition, a peptide mimetic can act as an inhibitor, but, by definition, is not a dominant negative mutant of any natural protein. Applicants do not provide their own definition of the term "dominant negative mutant" and the definition used in art defines a dominant negative mutation as an inactivation mutation of a gene whose mutant protein products interferes with the function of the normal gene product from the other allele; see the enclosed copy of the relevant page of *Molecular Biology and Biotechnology. A Comprehensive Desk Reference*, Meyers R. ed. Wiley-VCH 1995.

Claim 11, 13-17 are rejected for the use of indefinite phrases "means that inhibits", "means for inhibiting", "means for binding" and "inhibition means" that are not defined in the disclosure. The examiner suggests the language: inhibits or binds.

Claim 14 is confusing as to the function of a dominant negative mutant. The claimis directed to a peptide which is a dominant negative mutant of human telomerase "but which lacks telomerase activity". By definition a dominant negative mutant lacks telomerase activity.

The limitation "deletions consisting essentially" in claim 1-3, 5-7, 16 and 17 makes the claims indefinite, because it is unknown which deletions of which amino acidsof SEQ ID NO:2 are additionally included/excluded form the scope of the claim. The phrase "deletions consisting essentially of" is for the purpose of searching and

applying prior art construed as equivalent to "comprising"; see MPEP 2111. 03 "Transitional Phrases", copy enclosed.

3.2. 35 USC, section 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3.2.1. Lack of written description

Claims 1-3, 5-7 and 10-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a large and variable genus of polypeptides, and methods of their use, for which the description of structure is insufficient or lacking. The polypeptides are as follows:

Claim 1. A polypetide that comprises at least 10 consecutive amino acids from a sequence encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a sequence complementary to SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565, residues 930-934, or deletions consisting of at least 10 consecutive amino acids from residues 323-450,637-660, 748-766, 1055-1071, or 1084-116 of SEQ ID NO: 2.

Claim 2. As claim 1.

Claim 3. A polypeptide comprising at least 25 consecutive amino acids of SEQ ID NO: 2 wherein SEQ ID NO: 2 contains one or more deletions consisting essentially of residues 560-565, 930-934, 323-450, 635-660, 748-766, 1055-1071, or 1084-1116.

Claim 5. A polypeptide that comprises at least 10 consecutive amino acids from a sequence encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a sequence complementary to SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565, residues 930-934, or deletions consisting of at least 10 consecutive amino acids from residues 323-450,637-660, 748-766, 1055-1071, or 1084-116 of SEQ ID NO: 2, wherein said polypeptide is a dominant negative mutant.

Claim 6. A polypetide that comprises at least 10 consecutive amino acids from a sequence encoded by a polynucleotide that hybridizes under stringent

conditions to a polynucleotide consisting of a sequence complementary to SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565, residues 930-934, or deletions consisting of at least 10 consecutive amino acids from residues 323-450,637-660, 748-766, 1055-1071, or 1084-116 of SEQ ID NO: 2, wherein said polypeptide is a dominant negative mutant and wherein said polypeptide binds RNA component but lacks processive telomerase activity.

Claim 7. A polypetide that comprises at least 10 consecutive amino acids from a sequence encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a sequence complementary to SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565, residues 930-934, or deletions consisting of at least 10 consecutive amino acids from residues 323-450,637-660, 748-766, 1055-1071, or 1084-116 of SEQ ID NO: 2, wherein said polypeptide is a dominant negative mutant and wherein said polypeptide binds human telomers but lacks processive telomerase activity.

Claim 10. A method of inhibiting telomerase catalytic activity, comprising introducing a protein, peptide, or peptide mimetic according to claim 1 into an environment containing telomerase reverse transcriptiase.

Claim 11. A method of inhibiting telomerase catalytic activity, comprising introducing into an environment containing telomerase reverse transcriptase and

telomerase RNA component a means that inhibits binding of the transcriptase to the RNA component.

Claim 12. A method of inhibiting telomerase catalytic activity in a cell, comprising expressing in the cell a nucleic acid encoding a protein or peptide according to claim 2.

Claim 13. A peptide which is a dominant negative mutant of human telomerase.

Claim 14. A peptide which is a dominant negative mutant of human telomerase, wherein said mutant binds telomerase RNA, but lacks telomerase catalytic activity.

Claim 15. A peptide which is a dominant negative mutant of human telomerase, wherein said mutant does not bind RNA component.

Claim 16. A peptide which is a dominant negative mutant of human telomerase exerting inhibition of telomerase by its fragment that comprises at least 10 consecutive amino acids from a sequence encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of a sequence complementary to SEQ ID NO: 1; but which contains one or more deletions consisting essentially of residues 560-565, residues 930-934, or deletions consisting of at least 10 consecutive amino acids from residues 323-450,637-660, 748-766, 1055-1071, or 1084-116 of SEQ ID NO:2.

Claim 17. A peptide which is a dominant negative mutant of human telomerase exerting inhibition of telomerase by its fragment that comprises at least 25 consecutive amino acids from SEQ ID NO: 2, which contains one or more deletions consisting essentially of residues 560-565, residues 930-934, or deletions consisting of at least 10 consecutive amino acids from residues 323-450,637-660, 748-766, 1055-1071, or 1084-116 of SEQ ID NO: 2.

Claims 1, 2, 3, 5, 6, 7, 10, 12, 16 and 17 are directed to a large and variable genus of polypeptides of stated function, or methods of use thereof, for which the structure is insufficiently described. The disclosure provides representative species that are polypeptides identified by SEQ ID NO: 2, wherein amino acids residues 560-565, 930-934, 323-450, 637-660, 748-766, 1055-1071, or 1084-1116 of SEQ ID NO: 2 are deleted. Providing these species is insufficient for identifying the structure of the all species of the genus, because their structural features do not identify the whole genus of polypeptides. Polypeptides comprising only at least 10/25 consecutive amino acids of representative species consists not only of these at least 10/25 consecutive amino acids, but also other amino acid/amino acid sequences of unknown structure and position in a claimed polypeptide. For example, a polypeptide of 300 amino acids comprising 10 amino acids which are residues 510-519 of SEQ ID NO: 2 and completely coincidental 290 amino acids is within the scope of the claims if it inhibitds human telomerase, but the structure of the 290 additional amino acids necessary for such a protein to have the claimed function is not disclosed.

Because of lack of structural characteristics of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 13-15 are directed to any dominant negative mutant, natural or man-made, of any human telomerase reverse transcriptase or to any dominant negative mutant that lacks telomerase catalytic activity, but retains the capability of binding telomerase RNA component or any dominant negative mutant that lacks telomerase catalytic activity and capability of binding telomerase RNA component and claim 11 is drawn to method of use of such proteins as well as other compounds which inhibits binding of telomerase reverse transciptase to telomerase RNA. The claims are generic; they are directed to large and structurally diversified genus of dominant negative mutants for which the disclosure does not provide sufficient structural description. Applicants disclose several mutants of human telomerase derived from telomerase of SEQ ID NO: 2 by deleting its particular fragments, wherein said mutants are catalytically inactive or catalytically inactive and not binding telomerase RNA (for example deletion 192-450 and 560-565); see Table 1 of the specification. Structurally, these mutants are not representative species of the claimed genus of all possible dominant negative mutants of all human telomerase reverse transcriptases, because they do not provide identifying structural characteristics of the whole genus. Those skilled in the art are aware of existence of dominant mutants of human telomerase whose structure is different from those claimed by Applicants; see for example papers by Killian et al,

1997, Harrington et al 1997 and Weinrich et al. 1997, all enclosed in the information disclosure statement). Currently the full genomic sequence of the human telomerase reverse transcriptase, hTERT, has been disclosed (Wick, et al, Gene, 1999, 232, 97-106, copy enclosed). The complete gene consists of 16 exons and 15 introns. In addition, the length of introns currently numbered as 2, 6 and 12 is variable (Leem et al. Oncogene, 2002, 21, 769-777, copy enclosed), because these introns comprise tens of allelic forms. Thus SEQ ID NO: 2 is not the only sequence identifying the functional human telomerase. The complexity of structure and splicing of human telomerase is greater that that disclosed by Applicants in the early studies of the gene and its expression, therefore, the Applicants claim to all dominant negative mutants of human telomerase include subject matter not disclosed nor described in the specification. In conclusion, those skilled in the art realize that the genus of dominant negative mutants of human telomerase encompasses larger scope of structures than those disclosed by Applicants.

Because of lack of structural characteristics of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

3.2.2. Scope of enablement

Claims 1, 2, 3, 5, 6, 7, 10-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for dominant negative mutants having

the amino acid sequence derived from SEQ ID NO: 2 wherein the amino acids 192-450 or 637-660 or 638-66 or 748-766 or 748-764 or 1055-1071 or 1084-116 or 650-565 are deleted, or methods of their use, does not reasonably provide enablement for any peptide that inhibits human telomerase or any dominant negative mutant of human telomerase, and their use, as claimed in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to the large number of peptide inhibitors of human telomerase and dominant negative mutants of human telomerase; see the above rejection for lack of written description. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any peptide fragment of human telomerase that inhibits human telomerase or is a dominant negative

mutant of any human telomerase obtained from human tissues or man-made and methods of use thereof.

While methods of gene cloning and gene structure manipulations are well known in the relevant art, and skills of the artisans highly developed, one skilled in the art is not able to make any dominant negative mutant of human telomerase because the lack sufficient structural characteristics of said mutants makes the probability of success in obtaining the claimed invention very low. Thus, to make and use the claimed invention one skilled in the art is forced to do research outside the realm of routine experimentation. If a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that the claimed species have the functionality intended by Applicants. The provision of dominant negative mutants having the amino acid sequence derived from SEQ ID NO: 2 by deleting the amino acids 192-450 or 637-660 or 638-66 or 748-766 or 748-764 or 1055-1071 or 1084-116 or 650-565 fails to provide such guidance of the structure of any polypeptide which remain encompassed within the scope of the rejected claims.

Examiner concludes that without the further guidance on the part of Applicants in regards to structure of the claimed polypeptides, experimentation left to those in the art is improperly extensive and undue.

4. Conclusion

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (571) 272-0944 and the right fax number is (571) 273-0944. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m. EST.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner